CLAIMS

1. Process for detecting an allosteric effector of a receptor, by determination of the variation:

– in the dissociation and/or association kinetics of the complex formed between the abovementioned receptor and one of its ligands in the presence of said allosteric effector, relative to the dissociation and/or association kinetics of the complex formed between said receptor and said ligand, in the absence of said effector,

– and/or in the amplitude of the bond formed between the abovementioned receptor and one of its ligands in the presence of said allosteric effector, relative to the amplitude of the bond formed between said receptor and said ligand, in the absence of said effector,

provided that when the variation in the abovementioned amplitude is negative, the existence of the variation in the abovementioned kinetics is also detected,

said receptor and said ligand being involved in at least one biological response under appropriate physiological conditions, and the allosteric effector being capable of modulating at least one of the responses,

said receptor being marked by a fluorescent protein chosen from the fluorescent proteins obtained or derived from autofluorescent proteins of cnidaria, the molecular extinction coefficient of which is greater than approximately $14000M^{-1}.cm^{-1}$ and the fluorescence quantum efficiency is greater than approximately 0.38,

said ligand being marked by a marker constituted:

– either by a molecule capable of absorbing the light emitted by the fluorescent protein,

– or by a fluorescent substance,

said determinations of variation in dissociation and/or association kinetics and of variation in amplitude being carried out by fluorescence energy transfer:

- between the abovementioned fluorescent protein and the abovementioned fluorescent substance, the fluorescent substance being such that either it is excitable at the emission wavelength of the abovementioned fluorescent protein, or it emits at the excitation wavelength of the abovementioned fluorescent protein, or

• between the abovementioned fluorescent protein and the abovementioned molecule capable of absorbing the light emitted by the fluorescent protein.

2. Process for detecting an allosteric effector of a receptor, by determination of the variation:

– in the dissociation and/or association kinetics of the complex formed between the abovementioned receptor and one of its ligands in the presence of said allosteric effector, relative to the dissociation and/or association kinetics of the complex formed between said receptor and said ligand, in the absence of said effector,

– and/or in the amplitude of the bond formed between the abovementioned receptor and one of its ligands in the presence of said allosteric effector, relative to the amplitude of the bond formed between said receptor and said ligand, in the absence of said effector, provided that when the variation in the abovementioned amplitude is negative, the existence of the variation in the abovementioned kinetics is also detected,

said receptor and said ligand being involved in at least one biological response under appropriate physiological conditions, and the allosteric effector being capable of modulating at least one of the responses,

said receptor being marked by a fluorescent protein chosen from:

– green fluorescent protein (GFP or EGFP), cyan fluorescent protein (CFP or ECFP), yellow fluorescent protein (YFP or EYFP) or GFPUV, or,

– variants derived from GFP, CFP, YFP or GFPUV, by addition, deletion or substitution of one or more amino acids, provided that these variants preserve the property of fluorescence,

– or fragments of GFP, CFP, YFP or GFPUV, or fragments of the abovementioned variants, provided that these fragments preserve the property of fluorescence,

said ligand being marked by a marker constituted:

– either by a molecule capable of absorbing the light emitted by the fluorescent protein,

– or by a fluorescent substance,

said determinations of variation in dissociation and/or association kinetics and variation in amplitude being carried out by fluorescence energy transfer:

- between the fluorescent protein as defined above and the abovementioned fluorescent substance, the fluorescent substance being such that either it is excitable at the emission wavelength of the fluorescent protein, or it emits at the excitation wavelength of the fluorescent protein, or
- between the fluorescent protein as defined above and the abovementioned molecule capable of absorbing the light emitted by the fluorescent protein.

3. Process according to claim 1 or 2, characterized in that the variation:

– in the dissociation kinetics of the complex formed between the abovementioned receptor and one of its ligands in the presence of said allosteric effector, relative to the dissociation kinetics of the complex formed between said receptor and said ligand, in the absence of said effector,

– and/or in the amplitude of the bond formed between the abovementioned receptor and one of its ligands in the presence of said allosteric effector, relative to the amplitude of the bond formed between said receptor and said ligand, in the absence of said effector

is determined.

4. Process according to one of claims 1 to 3, characterized in that only the dissociation kinetics of the complex formed between the abovementioned receptor and one of its ligands in the presence of said allosteric effector, relative to the dissociation kinetics of the complex formed between said receptor and said ligand, in the absence of said effector are determined.

5. Process according to one of claims 1 to 3, characterized in that only the amplitude of the bond formed between the abovementioned receptor and one of its ligands in the presence of said allosteric effector, relative to the amplitude of the bond formed between said receptor and said ligand, in the absence of said effector is determined.

6. Process according to one of claims 1 to 5, characterized in that the ligand is an antagonist.

7. Process according to one of claims 1 to 5, characterized in that the ligand is an agonist.

8. Process according to claim 1 to 3, by determination of:

– the variation in the amplitude of the bond formed between the abovementioned receptor and one of its ligands in the presence of said allosteric effector, relative to the amplitude of the bond formed between said receptor and said ligand, in the absence of said effector,

– and optionally the variation in the dissociation kinetics of the complex formed between the abovementioned receptor and one of its ligands in the presence of said allosteric effector, relative to the dissociation kinetics of the complex formed between said receptor and said ligand, in the absence of said effector.

9. Process according to claim 8, characterized in that only the variation in the amplitude of the bond formed between the abovementioned receptor and one of its ligands in the presence of said allosteric effector, relative to the amplitude of the bond formed between said receptor and said ligand, in the absence of said effector, when said variation is positive is determined.

10. Process according to claim 8, characterized in that:

– the variation in the amplitude of the bond formed between the abovementioned receptor and one of its ligands in the presence of said allosteric effector, relative to the amplitude of the bond formed between said receptor and said ligand, in the absence of said effector is determined,

and that said variation is negative, which requires the determination of:

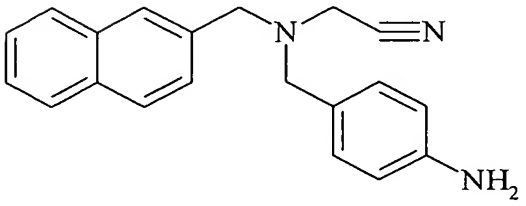
– the variation in the dissociation kinetics of the complex formed between the abovementioned receptor and one of its ligands in the presence of said allosteric effector, relative to the dissociation kinetics of the complex formed between said receptor and said ligand, in the absence of said effector.

11. Process according to claim 10, characterized in that said variation in dissociation kinetics is positive or negative, which implies that the compound tested is an allosteric effector.

12. Process according to claim 10, characterized in that said variation in dissociation kinetics is zero, which implies that the compound tested is a competitor.

13. Products corresponding to one of the following formulae:

A11



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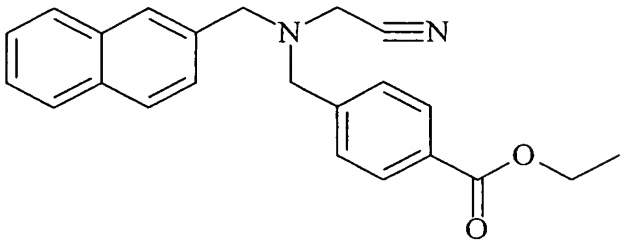

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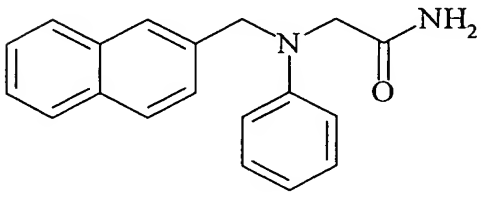

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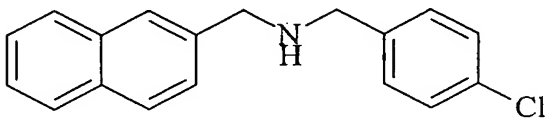

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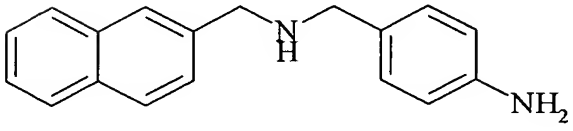

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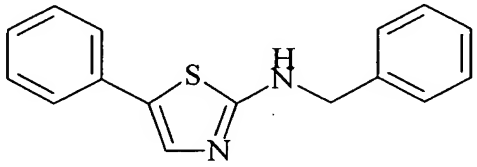

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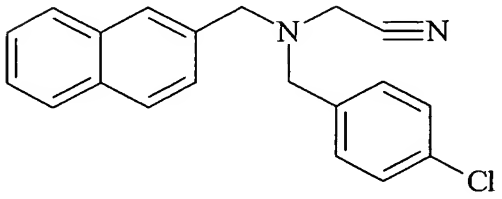

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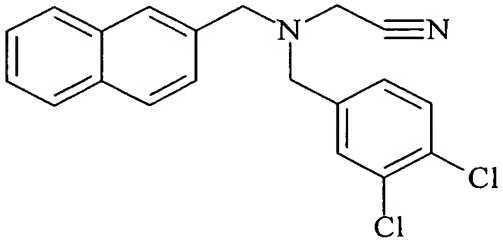

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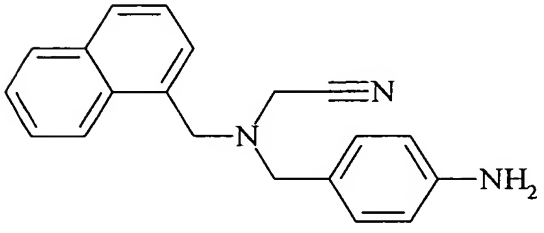

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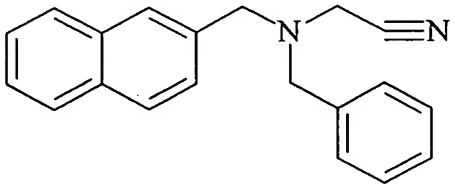

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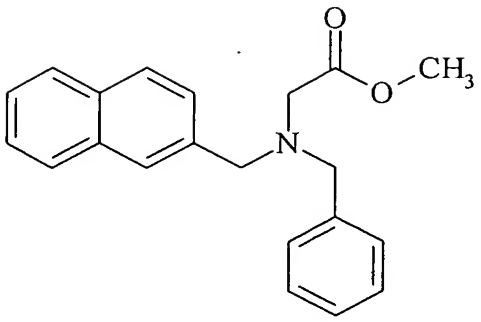

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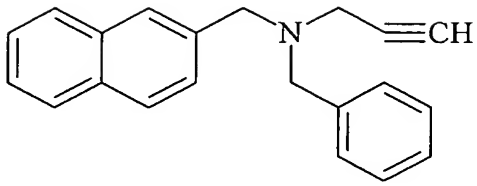

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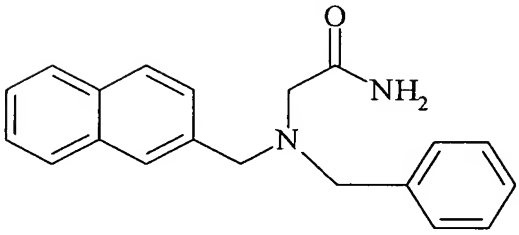

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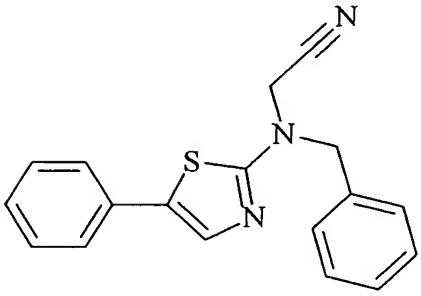

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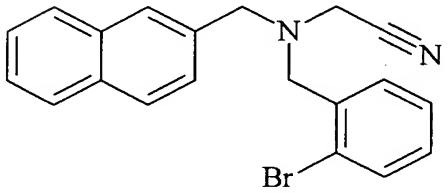

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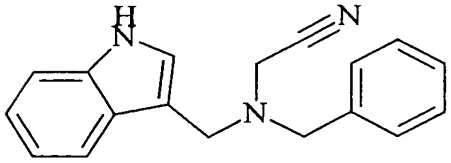

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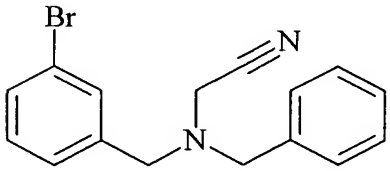

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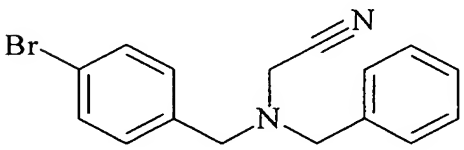

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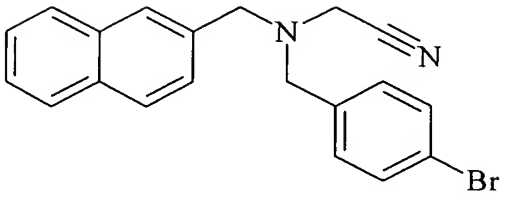

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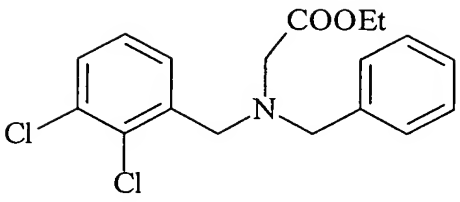

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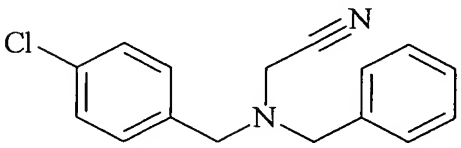

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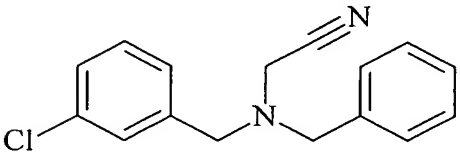

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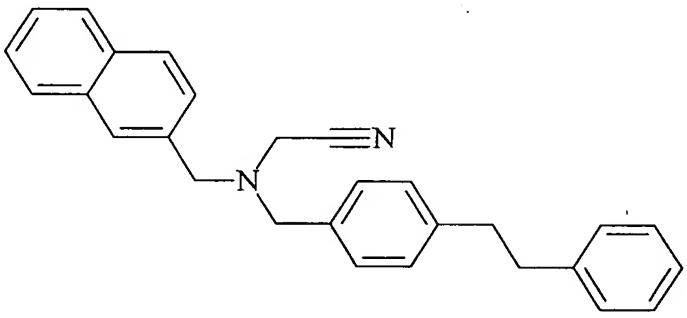

said products being compounds as detected by the process according to one of claims 1 to 12.